

REMARKS

Claims 1-7, 9-23, and 26-27 are pending in the application.

Claim Rejections

Double Patenting

Claims 1, 2, 4, 6, 16, 17, 19, 21, and 22 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 48-57 of United States Patent Number 6,268,142 (“the ‘142 patent”) in view of Bacus et al. (U.S. Patent Number 6,031,930; “Bacus”). Applicants traverse.

There is no suggestion to combine the ‘142 patent and Bacus to produce the claimed invention. Bacus teaches a method and apparatus for the analysis of neoplasia in tissue. This method is based upon a *morphological* analysis of tissue samples. Bacus does not teach the observation of a biomarker. In contrast, the present application provides a method identifying substances that modulate a subject’s inflammatory response by observing a biomarker in the presence and the absence of a test compound. The subject is administered an inducer prior to or concomitant with observing the biomarker. Furthermore, even if combined (which Applicants do not believe is proper) these references do not teach or suggest the invention as claimed.

According to the Examiner, claims 48-57 of the ‘142 patent disclose the chromosomal region IL-1RN and allele of IL-1A, and a biomarker selected from IL-1 alpha. The ‘142 patent does not teach the administration of an inducer to a test subject prior to or concomitant with observing the biomarker. The Examiner asserts that Bacus teaches the step of administering an inducer to a test subject prior to observing the biomarker. Applicants respectfully disagree.

Specifically, the Examiner cites Column 2, lines 17-47 of Bacus. This passage recites the need for the method and apparatus claimed in Bacus. This passage *does not teach*, as the Examiner asserts, observation of a biomarker prior to or concomitant with administration of an inducer to a test subject. In fact, this passage teaches that because of the *absence of biomarkers* for diagnosis neoplasm there is a need to develop *tests* (like morphological test disclosed on Bacus) for the measurement of neoplasia. “Currently, there are *no good objective biomarkers* for such diverse neoplasias that can be done using equipment. There is a *need to develop highly*

discriminating tests or measurements.” (Bacus, Column 2, lines 29-32, emphasis added). Thus, Bacus does not teach or disclose observing a biomarker.

The Examiner further cites Figure 15 and Column 17, lines 56 to Column 18, line 5 of Bacus. Figure 15 shows that the *morphologic* based method is capable of discriminating between normal tissue and cancer tissue at a very early stage. Esophageal cancer is induced by the administration of a carcinogen-- N-Nitrosomethylbenzamine. While Bacus administers an inducer to a subject for the sole purpose of causing cancer in the subject, Bacus does not teach observing a biomarker in the subject. In contrast, Bacus observes a morphologic change in the tissue.

Moreover, unlike the present invention, which observes and compares a biomarker in a *single subject* which has been further administered an inducer, Bacus observes and compares a morphologic change in a tissue sample from a subject that has been induced to have a cancer to a *second subject* that has not been induced to have cancer. Applicants request that this rejection be withdrawn.

35 U.S.C. § 103

A. Duff / Bacus

Claims 1-7 and 16-23 and 27 have been rejected as being obvious over Duff in view of Bacus. Applicants traverse.

For the reasons discussed above there is no suggestion to combine Duff and Bacus to produce the claimed invention. Furthermore, even if combined (which Applicants do not believe is proper) these references do not teach or suggest the invention as presently claimed. Applicants request that this rejection be withdrawn.

B. Duff/ Bacus/Girten

Claims 9-10 have been rejected as being obvious over Duff in view of Bacus and Girten et al (US Pat No. 5,760,001; “Girten”). Applicants traverse.

For the reasons discussed above there is no suggestion to combine Duff and Bacus to produce the claimed invention.

Girten does not cure these deficiencies. Girten teaches a method of “restraining” the biological activity of a cytokine to treat conditions resulting from elevated cytokine production, including disuse deconditioning, diabetes and glomerulonephritis, as well as cytokine-mediated

organ damage resulting from organ transplants or chemotherapy. Thus Girten teaches that a reduction of cytokine production may be useful in treating particular disease conditions associated with increased cytokine production. Girten does not teach a method of *identifying* a substance that reduces a biological response by observing a biomarker in a subject having exercise induced stress as required by claims 9 and 10.

C. Duff/ Bacus/Hallahan

Claims 11-15 have been rejected as being obvious over Duff in view Bacus and Hallahan et al. (U.S. Patent Number 5,962,424) ("Hallahan"). Applicants traverse.

For the reasons discussed above there is no suggestion to combine Duff and Bacus to produce the claimed invention.

Hallahan does not cure these deficiencies. Hallahan teaches a method for specifically targeting therapeutic and diagnostic agents to tumor vasculature by inducing E-selectin or L-selectin expression by x-ray irradiation or an oxidant. Hallahan, also teaches that monosodium urate crystal induces arthritis. Hallahan does not teach a method of *identifying* a substance that reduces a biological response by observing a biomarker in a subject, wherein the subject has an irritant (such as monosodium urate crystals) induced inflammatory response, as required by claims 11-15.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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